# Health and Retirement Study: Genetic Data Consortia Collaboration

Prepared by Jessica D. Faul and Jennifer A. Smith

Survey Research Center
University of Michigan
Ann Arbor, Michigan
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Genomics consortia bring together investigators and studies around the world to conduct meta-analyses of genome-wide genomic data on a range of behaviors, diseases, and traits. This model vastly increases the value of the HRS genetic resource by leveraging the increased power from larger sample sizes and producing replicable findings across a variety of harmonized phenotypes. Genetic variants that are common in populations usually have small individual effects on complex traits like behavior. The consortia model minimizes the likelihood of false-positive results in this context because they are well-powered and can apply stringent significance thresholds.

In order to conduct this work, each study that is part of a given consortium runs a genome-wide association study (GWA study, or GWAS) on the selected phenotype in their own sample using an analytic plan developed in partnership with other consortium investigators. GWAS is an examination of a genome-wide set of genetic variants in different individuals to see if any particular variant is associated with a given trait. GWAS typically focus on associations between single-nucleotide polymorphisms (SNPs) and traits. The results from the separate studies are then pooled in a meta-GWA at the consortium level.

HRS participates in a large and growing number of genomic consortia, including:

Cohorts for Health and Aging Research in Genetic Epidemiology (CHARGE)

Social Science Genetics Association Consortium (SSGAC)

Genetic Investigation of Anthropometric Traits (GIANT)

Continental Origins and Genetic Epidemiology Network (COGENT)

Global Lipids Genetics Consortium (GLCC)

GWAS and Sequencing Consortium of Alcohol and Nicotine Use (GSCAN)

Meta-Analyses of Glucose and Insulin-related traits Consortium (MAGIC)

Reproductive Genetics Consortium (ReproGen)

Runs of Homozygosity Genetics Consortium (ROHGen)

Stroke Genetics Network (SiGN)

Social Science Genetics Association Consortium (SSGAC)

The published results of these collaborations to date are listed below:

Barban, N., Jansen, R., de Vlaming, R., Vaez, A., Mandemakers, J. J., Tropf, F. C., . . . Mills, M. C. (2016). Genome-wide analysis identifies 12 loci influencing human reproductive behavior. *Nature Genetics, 48*(12), 1462-1472. doi:10.1038/ng.3698

Bihlmeyer, N. A., Brody, J. A., Smith, A. V., Lunetta, K. L., Nalls, M. A., Smith, J. A., . . . Arking, D. E. (2014). Genetic diversity is a predictor of mortality in humans. *BMC Genetics, 15*, 159. doi:10.1186/s12863-014-0159-7

Broer, L., Buchman, A. S., Deelen, J., Evans, D. S., Faul, J. D., Lunetta, K. L., . . . Murabito, J. M. (2015). GWAS of longevity in CHARGE consortium confirms APOE and FOXO3 candidacy. *Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 70*(1), 110-118. doi:10.1093/gerona/glu166

Davies, G., Armstrong, N., Bis, J. C., Bressler, J., Chouraki, V., Giddaluru, S., . . . Smith, J. A. (2015). Genetic contributions to variation in general cognitive function: a meta-analysis of genome-wide association studies in the CHARGE consortium (N=53 949). *Molecular Psychiatry, 20*(2), 183-192. doi:10.1038/mp.2014.188

Day, F. R., Ruth, K. S., Thompson, D. J., Lunetta, K. L., Pervjakova, N., Chasman, D. I., . . . Murray, A. (2015). Large-scale genomic analyses link reproductive aging to hypothalamic signaling, breast cancer susceptibility and BRCA1-mediated DNA repair. *Nature Genetics, 47*(11), 1294-1303. doi:10.1038/ng.3412

Demirkan, A., Lahti, J., Direk, N., Viktorin, A., Lunetta, K. L., Terracciano, A., . . . Räikkönen, K. (2016). Somatic, positive and negative domains of the Center for Epidemiological Studies Depression (CES-D) scale: a meta-analysis of genome-wide association studies. *Psychological Medicine, 46*(8), 1613-1623. doi:10.1017/s0033291715002081

Franceschini, N., Fox, E., Zhang, Z., Edwards, T. L., Nalls, M. A., Sung, Y. J., . . . Zhu, X. (2013). Genome-wide association analysis of blood-pressure traits in African-ancestry individuals reveals common associated genes in African and non-African populations. *American Journal of Human Genetics, 93*(3), 545-554. doi:10.1016/j.ajhg.2013.07.010

Joshi, P. K., Esko, T., Mattsson, H., Eklund, N., Gandin, I., Nutile, T., . . . Wilson, J. F. (2015). Directional dominance on stature and cognition in diverse human populations. *Nature, 523*(7561), 459-462. doi:10.1038/nature14618

Liu, C., Kraja, A. T., Smith, J. A., Brody, J. A., Franceschini, N., Bis, J. C., . . . Chasman, D. I. (2016). Meta-analysis identifies common and rare variants influencing blood pressure and overlapping with metabolic trait loci. *Nature Genetics, 48*(10), 1162-1170. doi:10.1038/ng.3660

Locke, A. E., Kahali, B., Berndt, S. I., Justice, A. E., Pers, T. H., Day, F. R., . . . Speliotes, E. K. (2015). Genetic studies of body mass index yield new insights for obesity biology. *Nature, 518*(7538), 197-206. doi:10.1038/nature14177

Marouli, E., Graff, M., Medina-Gomez, C., Lo, K. S., Wood, A. R., Kjaer, T. R., . . . Lettre, G. (2017). Rare and low-frequency coding variants alter human adult height. *Nature, 542*(7640), 186-190. doi:10.1038/nature21039

Matteini, A. M., Tanaka, T., Karasik, D., Atzmon, G., Chou, W.-C., Eicher, J. D., . . . Murabito, J. M. (2016). GWAS analysis of handgrip and lower body strength in older adults in the CHARGE consortium. *Aging Cell, 15*(5), 792-800. doi:10.1111/acel.12468

NINDS Stroke Genetic Network; International Stroke Genetics Consortium. (2016). Loci associated with ischaemic stroke and its subtypes (SiGN): a genome-wide association study. *Lancet Neurology, 15*(2), 174-184. doi:10.1016/S1474-4422(15)00338-5

Okbay, A., Baselmans, B. M. L., De Neve, J.-E., Turley, P., Nivard, M. G., Fontana, M. A., . . . Cesarini, D. (2016). Genetic variants associated with subjective well-being, depressive symptoms, and neuroticism identified through genome-wide analyses. *Nature Genetics, 48*(6), 624-633. doi:10.1038/ng.3552

Okbay, A., Beauchamp, J. P., Fontana, M. A., Lee, J. J., Pers, T. H., Rietveld, C. A., . . . Benjamin, D. J. (2016). Genome-wide association study identifies 74 loci associated with educational attainment. *Nature, 533*(7604), 539-542. doi:10.1038/nature17671

Pattaro, C., Teumer, A., Gorski, M., Chu, A. Y., Li, M., Mijatovic, V., . . . Fox, C. S. (2016). Genetic associations at 53 loci highlight cell types and biological pathways relevant for kidney function. *Nature Communications, 7*, 10023. doi:10.1038/ncomms10023

Rietveld, C. A., Medland, S. E., Derringer, J., Yang, J., Esko, T., Martin, N. W., . . . Koellinger, P. D. (2013). GWAS of 126,559 individuals identifies genetic variants associated with educational attainment. *Science, 340*(6139), 1467-1471. doi:10.1126/science.1235488

Weiss, A., Baselmans, B. M. L., Hofer, E., Yang, J., Okbay, A., Lind, P. A., . . . Luciano, M. (2016). Personality Polygenes, Positive Affect, and Life Satisfaction. *Twin Research and Human Genetics, 19*(5), 407-417. doi:10.1017/thg.2016.65

For a complete list of consortia and publications resulting from these collaborations, see the HRS webpage: https://hrs.isr.umich.edu/about/collaborations/genetic-data-consortia. Several projects are in progress and will be added to this page upon publication.

For a more complete list of active consortia, see the WikiGenes catalog of GWAS consortia:

http://www.wikigenes.org/e/art/e/185.html;jsessionid=0B9FD9E23354B7ACE2D9C3ED819F10A3.jvm2